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## II.C.2.

- Fifteen CTR studies demonstrate that nicotine affects hormone secretion and endocrine functions involved in modulation of mood and behavior;<sup>555</sup>

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II.C.2.

- Nine CTR studies show that nicotine induces both arousal and calming effects;<sup>556</sup>

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## II.C.2.

- Nine CTR studies use an EEG to examine the effects of nicotine on brain waves;<sup>557</sup>
- Nine CTR studies investigate the physiological effects of nicotine on the brain and their time course;<sup>558</sup>

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II.C.2.

- Six CTR studies characterize the effect of nicotine on behavioral performance and cognitive function;<sup>559</sup>
- Six CTR studies research the general pharmacokinetics of nicotine;<sup>560</sup>

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## II.C.2.

- Five CTR studies describe the development of sophisticated techniques for determining the presence of nicotine in body fluids;<sup>561</sup>
- Four CTR studies evaluate plasma profiles of nicotine;<sup>562</sup>

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Hibberd AR, Gorrod JW, Enzymology of the metabolic pathway from nicotine to cotinine, *in vitro*, *Eur J Drug Metab Pharmacokinet* 1983;8:151-162.

Kershbaum A, Bellet S, Cigarette, cigar, and pipe smoking. Some differences in biochemical effects, *Geriatrics* 1968;23(3):126-134.

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## II.C.2.

- Four CTR studies research the factors affecting the onset and duration of nicotine's effects on the body;<sup>563</sup>
- Three CTR studies investigate the metabolic fate of nicotine;<sup>564</sup>
- Two CTR studies specifically investigate the enzymatic systems involved in nicotine metabolism;<sup>565</sup>
- Two CTR studies show that smokers metabolize nicotine faster than nonsmokers;<sup>566</sup>
- Two CTR studies examine the factors affecting the absorption of nicotine into the bloodstream;<sup>567</sup>

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<sup>563</sup> Domino EF, Electroencephalographic and behavioral arousal effects of small doses of nicotine: A neuropsychopharmacological study. The effects of nicotine and smoking on the central nervous system, *Ann N Y Acad Sci* 1967;142:216-244.

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<sup>566</sup> Hatchell PC, Collins AC, The influence of genotype and sex on behavioral sensitivity to nicotine in mice, *Psychopharmacology (Berl)* 1980;71(1):45-49.

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## II.C.2.

- Two CTR studies examine the distribution of nicotine to the brain;<sup>568</sup>
- Two CTR studies research the relationship of nicotine's physiological effects on the body to nicotine blood levels;<sup>569</sup> and
- One CTR study shows that there may be gender differences in the metabolism of nicotine.<sup>570</sup>

The results of the CTR-funded research show that nicotine has significant pharmacological effects on the body. In fact, numerous CTR studies demonstrate that nicotine produces pharmacological effects similar to those of other addictive substances. For example:

- Thirteen CTR studies demonstrate that nicotine, like other addictive drugs, acts on dopaminergic receptors in the brain to release dopamine, a chemical in the brain's reward system that reinforces the intake of certain substances;<sup>571</sup>

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<sup>567</sup> Haines CF Jr, Mahajan DK, Miljkovic D, *et al.*, Radioimmunoassay of plasma nicotine in habituated and naive smokers, *Clin Pharmacol Ther* 1974;16(6):1083-1089.

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<sup>570</sup> Jusko WJ, Role of tobacco smoking in pharmacokinetics, *J Pharmacokinet Biopharm* 1978;6(1):7-39.

<sup>571</sup> Abood LG, Lu X, Banerjee S, Receptor binding characteristics of a 3H-labeled azetidine analogue of nicotine, *Biochem Pharmacol* 1987;36(14):2337-2341.

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- Twelve CTR studies demonstrate that tolerance to nicotine occurs;<sup>572</sup>

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